

<b>Notice of Allowability</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/833,031	GILAD ET AL.	
	Examiner J. D. Schultz, Ph.D.	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS**. This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1.  This communication is responsive to 6 December 2004.
2.  The allowed claim(s) is/are 9-26.
3.  The drawings filed on 11 April 2001 are accepted by the Examiner.
4.  Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a)  All
  - b)  Some\*
  - c)  None
 of the:
  1.  Certified copies of the priority documents have been received.
  2.  Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3.  Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\* Certified copies not received: \_\_\_\_\_.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.  
**THIS THREE-MONTH PERIOD IS NOT EXTENDABLE**.

5.  A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
6.  CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
  - (a)  including changes required by the Notice of Draftsperson's Patent Drawing Review ( PTO-948) attached
    - 1)  hereto or 2)  to Paper No./Mail Date \_\_\_\_\_.
  - (b)  including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date \_\_\_\_\_.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

7.  DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

#### Attachment(s)

1.  Notice of References Cited (PTO-892)
2.  Notice of Draftsperson's Patent Drawing Review (PTO-948)
3.  Information Disclosure Statements (PTO-1449 or PTO/SB/08),  
Paper No./Mail Date 11 April 2001
4.  Examiner's Comment Regarding Requirement for Deposit  
of Biological Material
5.  Notice of Informal Patent Application (PTO-152)
6.  Interview Summary (PTO-413),  
Paper No./Mail Date \_\_\_\_\_.
7.  Examiner's Amendment/Comment
8.  Examiner's Statement of Reasons for Allowance
9.  Other \_\_\_\_\_.

**EXAMINER'S AMENDMENT**

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Allen Yun on February 14, 2005.

In the specification, at line 2 of paragraph 0001, "2000, which" has been changed to -- 2000, now U. S. Patent Number 6,528,262,--

In the claims, claim 9 has been changed to read as follows:

9. (Currently Amended) A method for detection of differential expression of natural antisense messenger RNA (mRNA), comprising:

- (a) separately obtaining polyA-mRNA-A molecules from cell population A and polyA-mRNA-B molecules from cell population B;
- (b) separately generating by a reverse transcription enzyme a population of single-stranded cDNA-A molecules from polyA-mRNA-A and a population of single-stranded cDNA-B molecules from polyA-mRNA-B, wherein the polydeoxythymidine containing oligonucleotide primer used to produce the cDNA-B molecules comprises a specific bacteriophage RNA polymerase promoter region close to its 5' terminus;

- (c) incubating the combined populations of single-stranded cDNA-A molecules and single-stranded cDNA-B molecules, under conditions allowing hybridization of sense cDNA molecules with antisense cDNA molecules, wherein each single-stranded antisense cDNA molecule that hybridizes has a segment complementary to the sense cDNA molecule and hybridizes thereto to form a hybrid molecule with a double-stranded segment;
- (d) treating the hybrid molecules with a DNA polymerase having a 5' to 3' polymerase activity and a 3' to 5' exonuclease activity to remove single-stranded non-hybridized segments of the hybrid molecule from 3' to 5' and to extend the double-stranded segment of the hybrid molecule 5' to 3' over an adjacent single-stranded segment as template, thereby forming a double-stranded molecule having the RNA polymerase promoter region close to one terminus;
- (e) using the double-stranded molecule as a template for the specific RNA polymerase to produce a population of RNA molecules;
- (f) labeling with a first label the RNA molecules produced in step (e);
- (g) labeling with a second label as control the polyA- mRNA-A molecules and/or the polyA-mRNA-B molecules of step (a);
- (h) mixing labeled RNA molecules from steps (f) and (g) and hybridizing them to a DNA microarray; and
- (i) identifying the genes on the microarray which are preferentially labeled with the labeled RNA molecules of step (f), wherein the genes so identified on the microarray are detected as differentially expressing natural antisense mRNA.

In claim 18, the second step "(i)" has been changed to --"(j)".

The following is an examiner's statement of reasons for allowance: The claims of the instant invention, drawn to methods of detecting differential expression of natural antisense messenger RNA, is considered to be free of the prior art. The closest prior art is that of U. S. Patent Number 5,891,636, which teaches methods of subtractive hybridization utilizing a primer which contains a T7 promoter region, followed by T7 based transcription of unhybridized mRNA's; the instant application is considered to be patentably different in that the instant method requires reverse transcription of two distinct cDNA populations, followed by hybridization of the two distinct cDNA populations formed, neither of which are taught or suggested by the '636 patent, which teaches hybridization of an RNA population with a cDNA population.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

***Conclusion***

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Douglas Schultz, Ph.D. whose telephone number is 571-272-0763. The examiner can normally be reached on 8:00-4:30 M-F.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on 571-272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

JDS

**Best Available Copy**

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